FEDERAL SECURITY AGENCY
PUBLIC HEALTH SERVICE

IN REPLYING, ADDRESS THE
USPHS Tbc. Research Lab.
411 East 69th Street
New York 21, N. Y.

April 6, 1953

Dr. Joshua Lederberg
Dept. of Genetics
College of Agriculture
University of Wisconsin
Madison 6, Wisconsin

Dear Joshua:

Enclosed is a copy of the addendum that you suggested I write. I don't know whether the J. Bact. would rather publish this as such or as a separate note, but I'll leave it up to them. I had hoped it would come out a good deal shorter, but it unfortunately seemed desirable to present both the genetic and the biochemical backgrounds in some detail, and neither is simple. The last sentence is based on my recollection of a conversation with Norton some months ago; I haven't had a chance to check this with him since he's off to visit you.

Any comments you and Norton would care to make would be welcome; I won't send this until I return from Chicago next week.

The experiments with sulfonamide resistance have been so disappointing that we've decided to abandon them, at least for the time being. The low ~~reversions~~ levels of resistance obtained could be scored consistently, ~~with the parent strain;~~ but most of the resistance disappeared in the course of carrying out ~~process~~ tests. There might be something important here for someone who wanted to work it out patiently, but I don't think it's for me. I'm really sorry for this outcome, as I was looking forward to collaborating with you on the heterozygote experiments.

With best personal regards,

Sincerely,

Bernie

Bernard D. Davis

BDD:ls

Addendum on genetic exchange in Salmonella. The experiments reported here have a bearing on the recent discovery of bacteriophage-mediated genetic exchange (Zinder and Lederberg, J. Bact. 64, 679, 1952). This phenomenon was first observed with a Salmonella strain (SW-279) which had developed a requirement for tyrosine plus phenylalanine at one mutational step (SW-240) and an additional requirement for tryptophan at a second step. All three requirements could be simultaneously eliminated by genetic transfer with appropriate filtrates of a strain possessing the complementary synthetic abilities. Yet in subsequent experiments with many other strains only one genetic factor could be transferred to any recipient cell. Zinder and Lederberg therefore suggested that the triple requirement of strain SW-279 might involve a single gene; and they pointed out that this interpretation was supported by biochemical evidence from this laboratory. It seems important to analyze this evidence, (which is contained in the present paper), since the original experiments were designed to select only the products of multi-factor exchange, and hence the fortunate use of this particular two-step mutant appears to have been essential for the discovery of this one-factor type of transmission.

All the available strains that require tyrosine plus phenylalanine have been shown to be incompletely blocked in one or another reaction in the sequence of common aromatic precursors, and increasingly complete blocks in the same sequence have been shown to result in successive additional requirements for tryptophan and for p-aminobenzoic acid (Davis, J. Bact. 64, 729, 1952). The tryptophan requirement produced by the mutation from SW-240 to SW-279 could therefore have arisen either

from a more complete block in the already partly blocked sequence of common precursors or from a specific block in tryptophan synthesis. This mutation actually must have involved a block in the common sequence, since we could show that SW-279 (but not SW-240) has a relative requirement for p-aminobenzoic acid in addition to its other requirements. These two strains are listed respectively in Table 3 of this paper as S170-279, a quadruple auxotroph, and S170-240, a double auxotroph.

It is further noted in Table 3 that these two strains have the same pattern of accumulation (Z2 plus a trace of shikimic acid). This fact is also consistent with the possibility that the two mutations in strain SW-279 involve the same reaction; and it practically excludes the possibility that the second mutation affected an earlier reaction than the first, since the second mutation should then have prevented Z2 accumulation. However, these accumulations do not exclude the possibility that the second mutation affected a later reaction than the first. The available observations therefore support, but do not establish, the view that the two mutations in strain SW-279 involve the same reaction, and hence presumably the same gene. This view is further supported by the isolation of one-step prototrophic reversions from this strain (Zinder, personal communication).